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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,417	KHAMAR, BAKULESH MAFATLAL	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/1/10 & 2/2/10*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 37-72 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 37-72 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/1/10 and the Supplemental of 2/2/10 has been entered.

Claims 39-67 and new claims 70-72 are currently pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 37-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37, 66 and 69 are vague and indefinite because the metes and bounds of the solvent extracts recited in part (c) or the sonciated cell in part (b) cannot be understood. There are no method steps for obtaining the various solvent extractions recited in the instant claims or the instant specification. The components of the extract would be expected to vary based on the method steps used. Accordingly, it is unclear which actual extract possesses any of the therapeutic properties and it is unclear of the structure of the composition to be used in the method since its properties appear to be

variable. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Appropriate correction and/or clarification is requested.

Response to Applicant's arguments:

Applicants have argued that the scope of "sonicated" or "solvent extracts" of Mycobacterium w would have been readily understood by the skilled person. They argue that the term "solvent extract" is known in the art to refer to the separation of materials of different chemical types and solubilities by selective solvent action. In other words, a solvent extract of Mycobacterium w covers components selectively dissolved in solution when Mycobacterium w is treated with the specific solvents recited in the claim. The claims specifically recite that the solvent extraction is performed using one of a few organic solvents: chloroform, ethanol, methanol, acetone, phenol, isopropyl alcohol, acetic acid, urea, or hexane. See specification at, e.g., page 10. The specification further describes exemplary compositions of solvent extracts prepared with 1×10^{-x} Mycobacterium w cells treated with either methanol, chloroform, acetone or ethanol. See specification at, e.g., pages 6 and 7. These arguments have been fully and carefully considered but are not deemed persuasive. As stated above, there are no method steps for obtaining the various solvent extractions recited in the instant claims or the instant specification. The components of the extract would be expected to vary

based on the method steps used. Accordingly, it is unclear which actual extract possesses any of the therapeutic properties and it is unclear of the structure of the composition to be used in the method since its properties appear to be variable. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims.

Claim 70 is vague and confusing due to the phrase "administered by intradermally". It appears the phrase should be change to "administered intradermally".

Claim Objections

3. Claims 37, 66 and 69 are objected to because of the following informalities:

It appears to be in improper Markush format. Ex parte Markush sanctions claiming a genus expressed as a group consisting of certain specified materials. Inventions in metallurgy, refractories, ceramics, pharmacy, pharmacology and biology are most frequently claimed under the Markush formula but purely mechanical features or process steps may also be claimed by using the Markush style of claiming. See Ex parte Head, 214 USPQ 551 (Bd. App. 1981); In re Gaubert, 524 F.2d 1222, 187 USPQ 664 (CCPA 1975); and In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980). **It is improper to use the term "comprising" instead of "consisting of."** Ex parte Dotter, 12 USPQ 382 (Bd. App. 1931). The claim should recite that the composition "is selected from the group consisting of:"

Appropriate correction is required.

Claim Rejections - 35 USC § 112-Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention - The claims are drawn to methods of treating cancer; improving the quality of life in a patient suffering from cancer; ameliorating symptoms associated with cancer comprising administration to a patient a pharmaceutical composition comprising an effective amount of heat killed *Mycobacterium w*, a solvent extract of *Mycobacterium w*, wherein the solvent is selected from chloroform, ethanol, methanol, acetone, phenol, isopropyl alcohol, acetic acid, urea, and hexane, or an enzymatic extraction of *Mycobacterium w* wherein the enzyme is selected from liticase and pronase.

The amount of direction/guidance/examples present -The instant specification in its present form, while reciting various preparations of Mycobacterium w, does not specify which of the types was actually utilized nor how much of the composition was administered in the recited Examples. Therefore, there is insufficient information to enable the instant claims. The required information to support the instant claims, at a

minimum, would be the actual composition administered to the patients (whole cells, disrupted cells, cell fractions, etc), the dosage administered, the route of administration, and the frequency of administration. The instant specification does recite 10 different preparations of Mycobacterium w pharmaceutical composition, i.e., heat killed whole cells, methanol extract, chloroform extract, sonicate, acetone extract, ethanol extract, and does not specify which of the types was actually utilized. Because of the wide variety of the composition preparations, the actual constituents in each of the pharmaceutical compositions also vary greatly. Thus, without knowing exactly which preparation was utilized, there is insufficient information to enable the instant claims which merely recite "a pharmaceutical composition comprising an effective amount of" either "Mycobacterium w" or "a" constituent of Mycobacterium w. Additionally, there are no method steps for the various solvent extractions recited. The components of the extract would be expected to vary based on the method steps used. Accordingly, it is unclear which actual extract possesses any of the therapeutic properties and it would take one of skill in the art undue experimentation to practice the invention as claimed.

Cancer treatment is an extremely unpredictable art with a solid statistical data required to support it. The instant specification shows only anecdotal evidence of a few isolated patients with various symptoms and does not recite the actual composition used or the amount. These isolated, independent anecdotal examples are not sufficient to enable the claimed methods. The anecdotal case studies contain so many different variables and factors it is unclear what is actually causing the different effects and if they can be attributed to the Mycobacterium w composition. None of the isolated

incidents are sufficient to support claims broadly drawn to method for treatment or management of any cancer, nor do they support a method for the amelioration of symptoms associated with any cancer or improvement in quality of life in a cancer patient.

Response to Applicants' Arguments:

Applicants argue that:

> In the clinical study described in Example 4, Case 1, a 0.1 mL dose was administered intradermally over the deltoid region at a frequency of once a week for three months. *See* the specification at page 11, lines 10-21. Example 5 teaches that a 0.1 mL dose administered intradermally at a frequency of once a month for two months is effective. *See* the specification at page 12, lines 12-27. Five patients with muscle invasive bladder cancer were effectively treated in the study described in Example 6 upon monthly intradermal deltoid injection of a 0.1 mL dose of *Mycobacterium w* for six months. *See* specification at pages 12-13. Example 8(a) discloses that the 0.1 mL *Mycobacterium w* dosage can be administered by intradermal injection one a week for two months followed by every 15 days for two months and monthly for two months for a duration of six months for effective treatment. The 0.1 mL Mycobacterium w dosage was administered intradermally over the deltoid region every 15 days for three months in Example 8(b). *See* specification at pages 13-14. Thus, the specification provides extensive disclosure relating to route and frequency of administration of *Mycobacterium w.*
>
> Further, there are well established techniques for determining an effective dose and route and frequency of administration. Accordingly, one of ordinary skill in the art could determine proper dosage amounts and routes and frequency of administration of the claimed compositions without undue experimentation.

These arguments have been fully and carefully considered but are not deemed persuasive. These passages recite a '0.1 mL dose' was administered, but is unclear exactly what was in the dose, e.g., the chemical composition. Further, it recites that 'five patients with muscle invasive bladder cancer were effectively treated". It is unclear what is encompassed by "effectively treated". The use of standard radiotherapy was also used. Accordingly, it is unclear whether the composition had any effect or if it was the radiotherapy which caused five patients to show reduced bladder lesions. Cancer

treatment is an extremely unpredictable art with a solid statistical data required to support it. The instant specification shows only evidence of a very few isolated patients with various symptoms and does not recite the actual composition in the methods. A direct correlation to the product administered and the symptoms achieved has not been shown, nor has a statistical portion of treated subjects been shown.

Applicants cite:

MPEP §2164.02 states:

[L]ack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement. A single working example in the specification for a claimed invention is enough to preclude a rejection which states that nothing is enabled since at least that embodiment would be enabled.

This has been fully and carefully considered but is not deemed persuasive in the instant case. Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect the composition used and the correlation of symptoms 3) the relative skill of those in the art is recognized as

quite high (post-doctoral level). With regard to (4) the nature of the invention and (5) the state of the prior art, these have been discussed above. One of skill in the art would require guidance, in order to make or use the compostions in the methods as instantly claimed.

Applicants also argue that the claims specify the particular 'form' of the Mycobacterium w to be used in the claimed methods. They argue that:

> With respect to the dosage amounts and route and frequency of administration, applicants respectfully submit that one of ordinary skill in the art could determine proper dosage amounts and routes and frequency of administration of the claimed compositions without undue experimentation. The specification provides significant guidance with respect to these parameters. For instance, the specification provides 10 exemplary 0.1 mL dosage compositions comprising various *Mycobacterium w* preparations. Heat killed whole cell *Mycobacterium w* is used in compositions A-C and J, at cell counts ranging from 0.5×10^7 - 0.5×10^9. Compositions D-I recite cellular extracts of *Mycobacterium w* obtained by subjecting $1 \times 10^{-}$ cells to the various processing steps detailed in the specification at, e.g., page 10, lines 3-19.

These arguments have been fully and carefully considered but are not deemed persuasive. The dosage amounts, product to be used, route and frequency of administration are not merely 'routine experimentation. Rather, it is akin to invention. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification,

reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." As stated in the rejection set forth above, the instant specification shows only anecdotal evidence of a few isolated patients with various symptoms and does not recite the actual composition used or the amount. These isolated, independent anecdotal examples are not sufficient to enable the claimed methods. The anecdotal case studies contain so many different variables and factors it is unclear what is actually causing the different effects and if they can be attributed to the Mycobacterium w composition. None of the isolated incidents are sufficient to support claims broadly drawn to method for treatment of any cancer, nor do they support a method for the amelioration of symptoms associated with any cancer or improvement in quality of life in a cancer patient.

Status of Claims:

No claims are allowed. The prior art has taught the *idea* of the use of Mycobacterium w in pharmaceutical compositions for treating leprosy and treating HIV; however, the prior art does not teach or suggest using a pharmaceutical composition of Mycobacterium w to treat cancer, improve the quality of life in a patient with cancer or a method of ameliorating symptoms associated with cancer.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

2/9/10